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FITCH EVEN TABIN AND FLANNERY
120 SOUTH LA SALLE STREET
SUITE 1600
CHICAGO, IL 60603-3406

EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,964	MATTERN, CLAUDIA	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 15-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks, amendments and terminal disclaimer filed on 10/14/08 filed on 10/03/08 are acknowledged.

2. New claim 22 was added.

3. Claims 1-13 and 15-22 are included in the prosecution.

Response to Arguments

Rejection of claims 1-6, 8, 13, 15-17 and 20 under 35 USC § 103(a)

4. Applicant's arguments see Page 5, filed 10/14/08, regarding the rejection of claims 1-6, 8, 13, 15-17 and 20 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) have been fully considered but are not persuasive.

Applicant argues that the Illum reference requires the use of additional water for the preparation of gelatin microspheres. Applicant argues that the various disclosures of the formation of different types of gel in the Illum reference require the addition of water for the gel formation. Applicant argues that the Ko reference also requires the addition of water while formulating oil-in-water emulsions.

This is not persuasive because the claim language does not exclude a formulation that contains water. Claim 1 recites: "a lipophilic formulation for nasal application comprising …" The term "comprising" is open language and means that the named elements are essential but other elements may be added and still form a construct within the scope of the claim (See MPEP 2111.03).

Applicant argues that water is not required in new claim 22 of the instant invention. Applicant argues that the claimed invention does not require the formation of three types of emulsion formulations nor the addition of water to form an emulsion in new claim 22.

Claim 22 was added by amendment and will be addressed in a new ground of rejection over newly found prior art reference Bechgaard et al. (US 5,397,771).

Therefore, the rejection of 05/05/08 is maintained.

Rejection of claim 7 under 35 USC § 103(a)

5. Applicant's arguments see Page 7, filed 10/14/08, regarding the rejection of claim 7 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) and further in view of Patel et al. (US 6,248,363) have been fully considered but are not persuasive.

Applicant argues that the Patel reference is directed to a solid dosage form for a wide variety of pharmaceutical compounds and that even though hydrophobic ingredients can be utilized, the hydrophobic ingredients may contain water in small amounts. Applicant argues that solvents that are identified as additives to the pharmaceutical composition also include water and that added water is not required in the formulation of claim 1 or claim 22 of the claimed invention.

This is not persuasive because the claim language does not exclude a formulation that contains water. Claim 1 recites: "a lipophilic formulation for nasal application comprising …" The term "comprising" is open language and means that the named elements are essential but other elements may be added and still form a construct within the scope of the claim (See MPEP 2111.03). The Patel reference is

used as a supporting reference for the teaching that oleoyl macrogolglycerides were known in the art to be used as surfactants and that their use improves the bioavailability of drugs. One of ordinary skill in the art would therefore use the oleoyl macrogolglycerides as surfactants in pharmaceutical compositions.

Claim 22 was added by amendment and will be addressed in a new ground of rejection over newly found prior art reference Bechgaard et al. (US 5,397,771).

Therefore, the rejection of 05/05/08 is maintained.

Rejection of claims 9-10, 12 and 18-19 under 35 USC § 103(a)

6. Applicant's arguments see Page 7, filed 10/14/08, regarding the rejection of claims 9-10, 12 and 18-19 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) and further in view of Dondeti (International Journal of Pharmaceutics 1996) have been fully considered but are not persuasive.

Applicant argues that claim 1 has been defined as not including added water. Applicant argues that the agents listed in the Dondeti reference typically contain water, for example solutions, suspensions and gels. Applicant argues that these dosage forms containing water are not claimed currently in Applicant's claimed invention.

This is not persuasive because the claim language does not exclude a formulation that contains water. Claim 1 recites: "a lipophilic formulation for nasal application comprising …" The term "comprising" is open language and means that the named elements are essential but other elements may be added and still form a construct within the scope of the claim (See MPEP 2111.03). The Dondeti reference is used as a supporting reference for the teaching that viscosity regulating agents such as

HPMC, methylcellulose and microcrystalline cellulose were known in the art to be used to affect nasal absorption of drugs. One of ordinary skill in the art would therefore use the materials such as HPMC, methylcellulose or microcrystalline cellulose as viscosity regulating agents in pharmaceutical compositions.

Applicant argues that claim 22 states that added water is not required in the formulation.

Claim 22 was added by amendment and will be addressed in a new ground of rejection over newly found prior art reference Bechgaard et al. (US 5,397,771).

Therefore, the rejection of 05/05/08 is maintained.

Rejection of claim 11 under 35 USC § 103(a)

7. Applicant's arguments see Page 8, filed 10/14/08, regarding the rejection of claims 9-10, 12 and 18-19 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) and further in view of Glass (US 5,897,894) have been fully considered but are not persuasive.

Applicant argues that the Glass reference contains non-analogous art, a description of a microwavable popcorn product. Applicant argues that this reference has no relevance to pharmaceutical products having formulations that can be administered in nasal cavities. Applicant argues that any teaching from this reference is not relevant to the claimed invention, nor does it provide any of the missing parts of the teachings of the previously recited references to reject the noted claim.

In response to applicant's argument that Glass is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was

concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Glass is used as a supporting reference for the teaching that silicon dioxide was known in the art to thicken oils or to increase the viscosity of oils. One of ordinary skill in the art would therefore use silicon dioxide as viscosity regulating agents for oils in any compositions and would be an obvious choice of materials during the process of routine experimentation based on the desired viscosity of the oily composition.

Therefore, the rejection of 05/05/08 is maintained.

Rejection of claims 1-8, 10-12, 15, 18-19 and 21 under nonstatutory obviousness type double patenting

8. Applicant's filing of the terminal disclaimer against Application No. 11/560,187 on 10/14/08 is acknowledged.

However, until the approval of the terminal disclaimer, the nonstatutory obviousness type double patenting rejection of 05/05/08 will be maintained.

New grounds

9. New grounds of rejection over newly found prior art reference Bechgaard et al. (US 5,397,771) are being made against claim 22 which was added by Applicant. Since this new ground of rejection was necessitated by Applicant's amendment, this action is made FINAL.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-6, 8, 13, 15-17 and 20-21 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998).

Please note that claim 21 was inadvertently left out of the rejection in the previous office action.

Claims are drawn to a lipophilic formulation for nasal application comprising: a) at least one sexual hormone drug in an amount of from 0.5 to 6.0% by weight; b) at least one lipophilic or partly lipophilic carrier, comprising at least one oil in an amount of between 60% and 98% by weight of the formulation; and c) a compound having surface tension decreasing activity in an amount effective for *in situ* generation of an emulsion upon contact of the formulation with water.

Illum teaches a drug delivery system that enhances the uptake of active drug material from the nasal cavity (Col. 1, lines 16-19). The active drugs that can be used in this drug delivery system include sex hormones (Col. 9, line 31). Absorption enhancing materials such as surface active agents are also taught (Col. 5, lines 47-50). A preferred material is … lysophosphatidylcholine produced from egg or soy lecithin (Col. 5, lines 38-39). Furthermore, “the drug to be administered to a mucosal surface in the … nose could be administered as a viscous solution” (Col. 5, lines 6-8). The drug delivery system comprises microspheres. An emulsification technique using “purified olive oil” (Col. 6, line 48) and “soybean oil” (Col. 7, line 40) was used in the preparation of these

microspheres. The microspheres are "made from materials that are known to swell in contact with water to form a gel-like layer with good bioadhesive properties" (Col. 3, lines 5-7).

Illum does not specifically teach a drug delivery system comprising testosterone.

Ko et al. teach emulsion formulations of testosterone for nasal delivery (Abstract). The formulation materials include vegetable oil and surfactants (Page 198, Materials). The formulations are prepared by emulsification of the oil phase (containing the lipophilic testosterone and soybean oil) with the aqueous phase (further containing a surfactant) (Page 199, Preparation of formulations).

It would have been obvious to a person with ordinary skill in the art at the time the invention was made to combine the drug delivery system for nasal delivery teaching of Illum with the emulsion formulation of testosterone teaching of Ko to arrive at a nasal delivery system for testosterone. The motivation for combining these references is provided by Illum, which includes sex hormones as drugs that could be used in a nasal drug delivery system. For example, Illum teaches that progesterone "when given by the nasal route … is absorbed effectively with a bioavailability similar to that for an intravenous injection…" (Col. 2, lines 12-13). Furthermore, since testosterone is a sex hormone that is lipophilic, the inclusion of oil to prepare an emulsion for enhancing the bioavailability of the testosterone and as a slow or sustained release agent would be obvious to a person with ordinary skill in the art.

Regarding instant claims 1, 5, 8 and 20-21, which disclose the weight percentages of components (b), (c) and the sexual hormone drug, a person with ordinary skill in the art would find it obvious over the teachings of Illum and Ko and

would modify the percentages of the formulation based on the required dosage and desired release profile, and the recited percentages are obvious variants unless there is evidence of criticality or unexpected results.

Regarding instant claims 2-4, the oil would have been obvious over the "purified olive oil" (Col. 6, line 48) and "soybean oil" (Col. 7, line 40) as taught by Illum.

Regarding instant claim 6, the lecithin would have been obvious over the lecithin taught by Illum (Col. 5, lines 38-39).

12. Claim 7 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) as applied to claims 1-6, 8, 13, and 14 above, and further in view of Patel et al. (US 6,248,363).

The teachings of Illum and Ko are stated above. The difference that Illum and Ko do not teach is the oleoyl macrogolglyceride as the surfactant.

Patel et al. teach that the bioavailability of drugs (like simvastatin) (Col 6, line 49) can be improved by their invention, which includes macrogolglycerides as the surfactant (Col 35, line 46, Col 65, lines 50-53, claim 16).

A person with ordinary skill in the art at the time the invention was made would have used a variety of macrogolglycerides for surfactants. These macrogolglycerides would include different fatty acid esters and oleoyl macrogolglyceride since it would be more compatible with humans. The motivation to use these surfactants would be to allow the emulsification and improve the bioavailability of poorly soluble, lipophilic drugs.

13. Claims 9-10, 12 and 18-19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of

Microencapsulation 1998) as applied to claims 1-6, 8, 13, and 14 above, and further in view of Dondeti (International Journal of Pharmaceutics 1996).

The teachings of Illum and Ko are stated above. The difference not taught by Illum in view of Ko is the viscosity-regulating agent.

Dondeti teaches formulation parameters that affect nasal absorption of drugs. The use of HPMC (hydroxypropyl methylcellulose) (Page 118), methylcellulose (Page 118), and microcrystalline cellulose (Page 125) is taught.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the drug delivery system for nasal delivery teaching of Illum with the emulsion formulation of testosterone teaching of Ko and further combine it with the use of HPMC, methylcellulose and microcrystalline cellulose as viscosity regulating agents, as taught by Dondeti, and produce the instant invention.

One of ordinary skill in the art would do this because viscosity regulating agents such as HPMC, methylcellulose and microcrystalline cellulose were known in the art to be used to affect nasal absorption of drugs. One of ordinary skill in the art would therefore use the materials such as HPMC, methylcellulose or microcrystalline cellulose as viscosity regulating agents in pharmaceutical compositions because Dondeti teaches that: “increased viscosity prolongs the retention time of drug in the nasal cavity…” (Page 119).

Regarding instant claims 9-10, 12 and 18-19, a person with ordinary skill in the art would modify the percentages of the formulation (specifically percentage of the viscosity regulating agent) in order to optimize the release profile and the recited

percentage is an obvious variant unless there is evidence of criticality or unexpected results.

14. Claim 11 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998), and further in view of Glass (US 5,897,894).

The teachings of Illum and Ko are stated above. The difference not taught by Illum in view of Ko is colloidal silicon dioxide as the viscosity-regulating agent.

Glass teaches that "liquid oils can be thickened to increase their viscosity (e.g. with silicon dioxide) (Col. 5, lines 46-48).

It would have been obvious to a person with ordinary skill in the art at the time the invention was made to combine the drug delivery system for nasal delivery teaching of Illum with the emulsion formulation of testosterone teaching of Ko, and further combine it with the thickening of oils by using silicon dioxide, as taught by Glass, and produce the instant invention.

One of ordinary skill in the art would do this because silicon dioxide was known in the art as a thickening agent, and would have been an obvious choice of materials by the experimenter.

15. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998), and further in view of Bechgaard et al. (US 5,397,771).

The teachings of Illum and Ko are stated above.

Illum and Ko do not expressly teach a lipophilic formulation for nasal application wherein no water is added to the formulation.

Bechgaard teaches that vehicles used for nasal administration of biologically active substances possess lipophilic properties (Col. 1, lines 40-48). The biologically active substances include testosterone (Col. 5, lines 39-40 and Col. 6, lines 43-44). The pharmaceutical preparation also comprises surfactants (Col. 7, lines 55-58). Hydrophobic (and lipophilic) agents including castor oil are disclosed (Col. 10, lines 64-66). An anhydrous vehicle used in the method of administering a biologically active substance is disclosed (Col. 34, claim 8, lines 39-40).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a drug delivery system for nasal delivery comprising high level of oil or lipophilic agents, as taught by Illum, combine it with the emulsion formulation of testosterone, as taught by Ko, further combine it with the teaching of an anhydrous composition for nasal delivery comprising oils and testosterone, as taught by Bechgaard, and produce the instant invention.

One of ordinary skill in the art would do this because preparing a composition suitable for nasal administration that is anhydrous and contains testosterone as the active agent, castor oil as the lipophilic agent and surfactants was known in the art, as evidenced by Bechgaard. One of ordinary skill in the art would combine this known technique with the teachings of Illum and Ko because Bechgaard teaches that an anhydrous formulation may be useful in chronic dosing (Col. 25, lines 67-68).

Regarding instant claim 22, the limitation of no water added to the formulation would have been obvious over the anhydrous composition taught by Bechgaard (Col. 34, claim 8, lines 39-40).

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-8, 10-12, 15, 18-19 and 21 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6-8, 10-12, 16, 18-21 and 24-25 of copending Application No. 11/560,187 ('187 hereinafter). Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims and claims of '187 are drawn to a formulation for nasal application comprising at least one hormone drug, at least one lipophilic or partly lipophilic carrier and at least one compound having surface tension decreasing activity, an amount effective for *in situ* generation of an emulsion upon contact of the formulation with water. The difference is that component (b) of instant

claim 1 recites the range of the lipophilic carrier as between 60% and 98% by weight of the formulation. It would be obvious to one of ordinary skill in the art to modify the percentage of the lipophilic carrier in the formulation for nasal application during the process of routine optimization. The recited percentage range would have been an obvious variant unless there is evidence of criticality or unexpected results.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

18. No claims are allowed.

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615